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Risk factors for peristomal pyoderma gangrenosum complicating inflammatory bowel disease $^{\diamondsuit, \diamondsuit, \diamondsuit}$

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KEYWORDS

Crohn's diease; Inflammatory bowel disease; Peristomal pyoderma gangrenosum; Ulcerative colitis

Abstract

Background and aims: Risk factors for peristomal pyoderma gangrenosum (PPG) are not well defined. The aim of this study was to evaluate risk factors associated with development of PPG. Methods: Both PPG patients and controls were obtained by searching a database of the Cleveland Clinic using the ICD-9 code from March 2005 to May 2011. The control group was selected by matching for underlying diseases and type of stoma in a ratio of 3:1. Univariate and multivariate analyses were performed.

Results: A total of 15 PPG cases and 45 controls were included. The mean age at the time of PPG diagnosis was 46.0 ± 14.4 years. The underlying disease was Crohn's disease in 7 patients (46.7%), ulcerative colitis in 7 (46.7%) and indeterminate colitis in 1 (6.7%). Eleven patients (73.3%) had end ileostomy, 3 (20.0%) had loop ileostomy and 1 (6.7%) had colostomy. Eleven patients (73.3%) had active intestinal disease. In multivariate analysis, female gender, the presence of concurrent autoimmune disorders, and a high body mass index (BMI) were significantly associated with the presence of PPG, with odds ratios of 8.385 (95% confidence interval [CI]: 1.496-46.982, p=0.015), 6.882 (95% CI: 1.438-32.941, p=0.016), and 9.895 (95% CI: 1.970-43.704, p=0.005), respectively. After a median follow-up of 12.8 (interquartile range: 7.9-20.1) months with appropriate therapy, PPG healed in 8 patients (53.3%) and improved in 7 (46.7%) patients, after treatment.

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Abbreviations: BMI, body mass index; CD, Crohn's disease; CI, confidence interval; EIM, extraintestinal manifestations; IBD, inflammatory bowel disease; IC, indeterminate colitis; IQR, interquartile range; IRB, institutional review board; OR, odds ratio; PPG, peristomal pyoderma gangrenosum; PSC, primary sclerosing cholangitis; UC, ulcerative colitis.

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Conclusions: Female gender, the presence of autoimmune disorders and a high BMI appeared to be associated with an increased risk for the development of PPG in IBD patients.

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1. Introduction

Pyoderma gangrenosum is an ulcerative, cutaneous condition, initially described in 1930.¹ The characteristic lesions are chronic and recurrent ulcerations with a well-defined, undermined, violaceous border. Fifty percent of cases are found to be associated with underlying systemic diseases, most commonly inflammatory bowel diseases (IBD), arthritis, polyarthritis and malignancy.^{2–4} Lower extremities are the most frequently affected area, though other parts of the body can also be involved.^{2,5} Pyoderma gangrenosum often starts with a painful nodule or pustule, and healing typically results in a weblike cribriform atrophic scar, which is vulnerable to further breakdown with minor irritation or trauma.⁶ Superimposed infection commonly occurs with the lesion.

As an uncommon subtype, peristomal pyoderma gangrenosum (PPG) develops close to an abdominal stoma, comprising about 15% of all cases of pyoderma gangrenosum. ^{3,7–9} Similar to pyoderma gangrenosum, PPG is often a diagnosis of exclusion. Cultures typically do not reveal pathogenic organisms, and histologic evaluation often demonstrates nonspecific inflammatory reaction characterized by dermal infiltration of neutrophils. Other etiologies can also result in peristomal ulceration, resembling PPG, such as stitch abscess, contact dermatitis, extension of underlying Crohn's disease (CD) and irritation from leaking feces. ^{2,10–12} Differential diagnosis of a peristomal ulceration sometimes is difficult, and misdiagnosis of PPG is not uncommon. ¹³ Studies evaluating predictors for the development of PPG are warranted to improve the diagnosis and management of PPG.

Previously reported potential risk factors associated with PPG included female gender, active underlying disease and extra-intestinal manifestations (EIM) of IBD. 14–18 However, the majority of the data are based on case reports and risk factors for PPG have not been systematically studied. The aim of this study was to evaluate the risk factors associated with PPG in IBD patients.

2. Materials and methods

2.1. Patients

This study was approved by the Cleveland Clinic Institutional Review Board (IRB). All eligible patients were identified by searching the database using the ICD-9 codes from March 2005 to May 2011. Both paper charts and electronic medical records were carefully reviewed to exact patients' demographic information, clinicopathological variables and outcomes of PPG.

2.2. Patient groups

In this case-control study, a consecutive of 15 PPG patients were identified as cases. The controls were selected by matching for underlying disease and type of stoma with a study to control ratio of 1:3.

2.3. Inclusion and exclusion criteria

In order qualify for the study, PPG patients needed to meet all the following inclusion criteria: (1) having peristomal ulcers caused by pyoderma gangrenosum; (2) having underlying IBD; and (3) regular follow up at our institution. Patients whose peristomal ulcers were caused by other etiologies, such as stitch abscess and contact dermatitis, were excluded.

Controls needed to meet all the following inclusion criteria: (1) having stoma; (2) being consistent with the matching criteria; and (3) regularly being followed up at our institution. Patients with a history of pyoderma gangrenosum were excluded.

2.4. Diagnosis and treatment of PPG

As shown by a previous study from our institution, ¹⁸ the diagnosis of PPG has predominantly been clinical and based on a classic presentation of painful, undermined peristomal ulceration. Biopsy of the ulcers was performed for the purpose of exclusion.

The choice of the treatment modality and the use of type of pharmaceutical agents were at the discretion of treating physicians/colorectal surgeons. However, the common practice pattern in our institution was that local wound care with intra-lesional injection of corticosteroids was used in localized, non-aggressive form of PPG; and additional systemic medication (corticosteroids and/or immunosuppressive agents) was often administrated for PPG refractory to local therapy or for an extensive and aggressive form of PPG. If the patient failed the first-line topical and systemic therapy, anti-TNF biological agents (infliximab, adalimumab, or certilizumab pegol) were used.

2.5. Demographic and clinical variables

Demographic and clinical variables evaluated in the study included age at the diagnosis of IBD, age at stoma construction, duration of IBD, duration of stoma, body mass index (BMI), gender, history of smoking or, excessive alcohol use, type of IBD, type of stoma, family history of IBD, concurrent autoimmune disorders, extraintestinal manifestations (EIM), significant comorbidities, history of drug allergy, history of tonsillectomy, pre-operation use of immunosuppressives, pre-operation use of biologics, pre-operation high platelet counts, indication for surgery, stoma complications and activity of underlying IBD.

Duration of IBD was defined as the time interval from the date of IBD diagnosis (i.e. preoperative diagnosis of ulcerative colitis [UC], indeterminate colitis, [IC] or CD) to the date of stoma construction. Duration of stoma was defined as the time interval from the date of stoma construction to the diagnosis of PPG for cases, and to the date of stoma closure or last follow-up for controls. Indeterminate colitis (IC) was defined as histopathological diagnosis on proctocolectomy specimens

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